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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,841	11/17/2000	Roger Briesewitz	STAN-130	8223

7590

07/30/2002

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EXAMINER

NAFF, DAVID M

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 07/30/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/716841

Applicant(s)

Briesewitz *ad*

Examiner

Hoff

Group Art Unit

1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 5/07/02
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1-50 is/are pending in the application.
- Of the above claim(s) 1-15 + 33-50 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 16-32 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5 filed 2/13/01
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

In a response of 5/07/02 to a restriction requirement of 3/27/02, applicants elected claims 16-22 of Group II and requested that Groups III and IV be included with group II. On reconsideration, Groups III and IV are included with group II.

5 Claims 1-15 and 33-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims examined on the merits are 16-32.

10 The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15 Claims 16-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Requiring an optional linker makes the claims unclear. A linker should be required only when intended to be present.

20 Requiring a modulated pharmacokinetic property as compared with a free drug control in claims 16, 23 and 28 is uncertain as to meaning and scope since the drug of the control is not required to be the same drug as contained by the bifunctional molecule.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

25 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said

subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Briesewitz et al (BD) in view of Nygren et al (WO 91/01743) and Pouletty et al (5,843,440).

The claims are drawn to modulating a pharmacokinetic property by administering a bifunctional molecule of less than 5000 daltons molecular weight consisting of a drug and a pharmacokinetic modulating moiety optionally jointed by a linker.

Briesewitz et al disclose affinity modulation of small-molecule ligands such as modulating drug-protein interaction (page 1953, right col, lines 3-5). A bifunctional molecule is created by chemically linking a ligand to interest to a another small molecule that binds the protein tightly to a second protein. When the ligand is presented to a target protein by a second protein, additional protein-protein interactions outside of the ligand-binding sites serve either to increase or decrease affinity binding (page 1953, abstract). The small-molecule ligand, pYEEI, which is a tetrapeptide that binds to the Fyn SH2 domain

is covalently linked to PK506 and SLF that are ligands for FKBP to provide two bifunctional molecules (page 1954, under RESULTS). Ligands that bind to SH2 domains have been explored as possible therapeutics for cancer, osteoporosis, and inflammation and as immunosuppressive agents
5 (page 1953, right col, last two sentences of the second paragraph)

Nygren et al disclose extending the half-life of a biologically active protein or peptide such as a drug by binding the drug to a polypeptide fragment capable of binding to a serum protein.

Pouletty et al disclose modulating pharmacokinetics with a
10 bifunctional reagent that is a conjugate of a binding member specific for a blood-borne target agent such as a drug (col 3, line 11) and a binding member specific for a long-lived blood associated entity (col 1, lines 40-49). The conjugates find therapeutic use by reducing effective concentration of free drug, modulating volume distribution of the drug,
15 targeting the drug to sites of enhanced immune response or facilitating drug clearance from the blood stream (abstract and col 2, lines 23-260.

It would have been obvious to use a small-molecule drug as the small-molecule ligand of Briesewitz et al to target the drug to a desired target protein such as the SH2 domain as a therapeutic as suggested by
20 Briesewitz et al and to modulate a pharmacokinetic property such as half-life of the drug and volume distribution of the drug as suggested by Nygren et al and Pouletty et al. Modulating half-life and volume distribution of a drug would have inherently modulated hepatic first-pass metabolism as in claim 28.

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Art Unit: 1651

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on Monday-Thursday and every other Friday from about 8:30 AM to about 6:00

5 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number


10 (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist

15 whose telephone number is (703) 308-0196.

20 DMN
7/29/02


DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 12657